UNITED S[illegible] S DEPARTMENT OF COMMERCE
Patent and [illegible]ademark Office
[illegible] COMMISSIONER OF PATENTS AND TRADEMARKS

EXAMINER

ART UNIT	PAPER NUMBER
[illegible]14	15

DATE MAILED: [illegible]

This is a communication from the examiner in charge of your application
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on Paper #14 filed Sept. 29, 1997

■ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 (three) month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-17 is/are pending in the application
Of the above, claim(s) 4-10 is/are withdrawn from consideration
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-3 and 11-17 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-17 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 12
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

Response to Amendment

1 Applicants' amendment, filed September 29, 1997, has been entered and considered. Claims 18-45 have been canceled. Claims 1-17 remain pending with claims 4-10 withdrawn from consideration as being directed to non-elected species.

Objections/Rejections Withdrawn

2 In light of Applicants' amendments to the specification, the previous objection concerning reference signs shown in the drawings is withdrawn.

3 In light of Applicants' amendments to the claims, the previous rejection of claims 2 and 3 under 35 U.S.C. § 112, second paragraph, concerning abbreviations is withdrawn.

4 Upon review of the specification as a whole and the requirements that terms be read in light of the specification and given the broadest reasonable interpretation in the relevant art, the previous rejection of claims 1-3 and 11-17 under 35 U.S.C. § 112, second paragraph concerning "receptor protein" is withdrawn.

5. In view of the immediately preceding paragraph, the previous rejection of claims 1, 11, 13 and 14 under 35 U.S.C. 102(b) as being anticipated by Maddon et al. is withdrawn.

6. In light of amendments to the claims, the previous rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Gannon et al. is withdrawn.

Claim Rejections - 35 U.S.C. § 112

7. Claims 1 and 11-17 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the disclosed viral proteins, does not reasonably provide enablement for any viral protein "required for viral infection, replication, assembly or release". This rejection has been explained in the previous Office Action. Applicants' arguments have been fully considered but they are not deemed to be persuasive. Applicants argue that Phizicky et al. (Exhibit B) demonstrates that the general state of the art at the priority date of the instant application included basic techniques for identifying protein-protein interactions; that the interactive trap (two-hybrid) system is one exemplary method; and that Phizicky et al. indicate that "the art has met the challenge of identifying and characterizing various protein-protein interactions".

Without addressing whether Phizicky et al. is appropriate for indicating the general state of the art at the priority date of the instant application, the Examiner notes that they do state that with regard to the "two-hybrid system", "it can be used to detect interactions between candidate

proteins whose genes are available by constructing the appropriate hybrids and testing for reporter gene activity" (see page 105, first full paragraph). Thus the guidance is that a skilled artisan can identify and characterize protein-protein interactions by picking one candidate protein and then screening other proteins against in to see if an interaction is found. The instant claims, however, are directed to identifying inhibitory peptides and small organic compounds by use of a system comprising any host cell protein and any viral protein "required for viral infection, replication, assembly or release". This requires the use of an established protein-protein interaction and then use of it in the methods to identify the inhibitors. Thus the experimentation required to practice the invention would first require the selection of either a candidate host cell protein or a candidate viral protein, determination of corresponding viral or host cell, respectively, proteins that interact with it, and then use of that interaction to identify inhibitors. It is the first required screening with candidate host cell proteins and candidate viral proteins that is not adequately enabled because it essentially requires the skilled artisan to test all host cell proteins against all viral proteins and all viral proteins against all host proteins without sufficient guidance, and little predictability in the art, as to what host or viral proteins to test. Thus while the actual repetitive testing for such interactions is possible in light of the art, mere repetitive experimentation in the absence of predictability or guidance does not equal routine, and thus not undue, experimentation because leaving the skilled artisan with the equivalent of a hunting license to go forth and look for additional appropriate protein-protein interactions does not constitute enablement

8. Claims 1-3 and 11-17 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the disclosed viral and host cell proteins, does not reasonably provide enablement for any protein or peptide "corresponding to the binding site" of such proteins. This rejection has been explained in the previous Office Action. Applicants' arguments are identical to those addressed above, have been fully considered and deemed not to be persuasive for the reasons above.

The Examiner notes that alteration of the claims to recite protein or peptide "fragment" comprising the binding site of the host cell protein or viral protein (in essence "fragment" plus a functional limitation on its activity without reciting "corresponding") would obviate this rejection. He further notes that this would also obviate the rejection under 35 U.S.C. 112, second paragraph below. Descriptive support for "fragment" appears to already be present in the language of claim 1 as originally filed.

9. Claims 1-3 and 11-17 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assays using the disclosed binding conditions, does not reasonably provide enablement for assays conducted "under conditions and for a time sufficient to permit binding and the formation of a complex". This rejection has been explained in the previous Office Action. Applicants' arguments have been fully considered but they are not deemed to be persuasive as they are identical to those addressed above.

As previously explained, it is *a priori* unpredictable as to which of the enormous number of possible assay conditions would result in interactions permitting interaction between two proteins. Even viewing the art in light of Phizicky et al., the skilled artisan would find that the guidance is to attempt to identify interactions at one or at most a few conditions with a candidate protein and see whether an interaction exists. The instant claims, however, require any interaction under any conditions so long as an interaction occurs. As previously explained, it is not routine in the art to attempt all possible conditions without sufficient guidance or predictability as to which conditions are more likely to allow productive interactions. This is particularly significant in the instant case since interactions with host cell proteins, which may only occur under unknown or ill defined localized cellular conditions, is required.

10. Claims 1-3 and 11-17 are again rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection has been explained in the previous Office Action. Applicants' arguments have been fully considered but they are not deemed to be persuasive. Applicants argue that page 20, lines 13-14 and page 21, lines 11-12 adequately define fragments as having binding activities, that the skilled artisan would not be confused as to what amino acids are encompassed, and that functionally equivalent sequences would not have very different consequences.

While the Examiner understands that the claims contain word suggesting a functional limitation requiring a binding activity, the instant rejection is based upon the use of the words "corresponding to" because the actual scope and definition of the phrase is not clearly defined in the specification and its common definition results in sufficient ambiguity to render the claim indefinite because it is unclear as to what characteristics are to determine whether a "correspondence" exists.

Contrary to Applicants' second assertion, the skilled artisan would be confused since a literal reading of the phrase in the context of claim 1 is that given a particular binding site, protein or peptides containing and amino acid sequence "corresponding to" the binding site are also encompassed. There is no limitation indicating that the "corresponding" protein or peptide must possess the binding activity. Since a myriad of possible interpretations of the phrase are possible, as previously explained, the scope of the language, and hence claims, is unclear.

Lastly, there are sequences that may be within the scope of the phrase which would not be expected to possess the required binding activity. For example, if amino acid composition is the critical characteristic meant by the phrase, it would be surprising to find that every peptide with the same amino acid composition (regardless of sequence) is sufficient to permit binding to either a host cell or viral protein.

The Examiner notes that he has suggested language to obviate this rejection above

11. Claims 1-3 and 11-17 are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection has not been previously made. The claims have been amended to refer to "small organic molecule" but the scope of that term is not defined in the specification. Since the term occurs with respect to test compounds to apply in the claimed assays, its definition is critical to the determination of the metes and bounds of the claimed invention. Without some definition of the limits of "small", the claim is indefinite.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Barik et al (AD).

Barik et al (AD) teach the use of casein kinase II (a host cell protein) to phosphorylate phosphoprotein P of vesicular stomatis virus (VSV), which is part of the viral RNA-dependent RNA polymerase that produces viral mRNAs (see entire document). They further teach the screening of antiviral drugs against casein kinase II *in vitro* as a means of identifying drugs that inhibit P protein phosphorylation and hence VSV infection (see page 6574, bridging paragraph

between left and right columns). Since such screening methods are within the scope of claim 1.

Barik et al.(AD) anticipate the claim.

14 Any inquiry concerning this communication or earlier communications should be directed to Kawai Lau whose telephone number is 703-308-4209. The examiner can normally be reached Monday-Friday from 7 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 703-308-4216. The fax phone number for Official Papers to this Group is (703) 305-4227. The fax phone number for Unofficial Papers to the Examiner is (703) 305-7401.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**robert.wax@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is 703-308-0196.

Kawai Lau, Ph.D.
December 22, 1997

Kawai Lau
Patent Examiner
Group 1800